Solvent Loss Minimization LS-III

LS-III Solvent Summary for Top 5 Products

1) Fresh 305 KL. (28%)

2) Column Distilled 347 KL. (32%)

3) Plant Distilled 440 KL. (40%)

4)

4) Target Saving Quantity 15 KL. (over all 5% of Fresh Consumption will be reduced).

5) Budget Requirement.

6) Pay back.

Fresh & RFS Solvent Input Details

Solvent Input / Batch Details in Commercial Products @ LS-III

S. No	Product	Stage	B.Size (kg)	Output (kg)	BCF (Hrs)	Total Time Cycle (Hrs)	No. of batches /month	Stage Cap (TPM)	Yield Factor	API Eq. Cap (TPM)	Solvent	Quantity in (Lt / Batch)				Quantity in %			Remarks
												Fresh	Column Distill	Plant Distill	Total	Fresh	Column Distill	Plant Distill	
1	Clopidogrel Bisulfate	CTPS1	400	825	24	72	28.0	23.1	0.6	14.6	Toluene (S-804)	0	0	1400	1400	0	0	100	
2											Cyclo Hexane (S-836)	0	400	1800	2200	0	18	82	
3		COPB1	1000	1260	36	168	18.7	23.5	0.6	15.0	Methanol (S-801)	4000	3500	0	7500	53	47	0	
4											MDC (S-807)	0	0	2700	2700	0	0	100	
5											Acetone (S-805)	80	1000	0	1080	7	93	0	
6		CGBH1	800	550	30	192	22.4	12.3	0.98	12.1	MDC (S-807)	0	0	1600	1600	0	0	100	
7											Toluene (S-804)	0	0	4650	4650	0	0	100	
8											IPA (S-806)	1200	1650	0	2850	42	58	0	
9											Ethyl Acetate (S-811)	1200	0	2100	3300	36	0	64	
10		CGBH2	500	498	72	144	9.3	4.6	--	4.6	Methanol (S-801)	750	0	0	750	100	0	0	
11											CH (S-836)	400	0	1600	2000	20	0	80	
12											Acetone (S-805)	1250	1700	0	2950	42	58	0	

PRODUCT	STAGE	BATCH SIZE	LOSS %	

Solvent Input / Batch Details in Commercial Products @ LS-III

S. No	Product	Stage	B.Size (kg)	Output (kg)	BCF (Hrs)	Total Time Cycle (Hrs)	No. of batches /month	Stage Cap (TPM)	Yield Factor	API Eq. Cap (TPM)	Solvent	Quantity in (Lt / Batch)				Quantity in %			Remarks
												Fresh	Column Distill	Plant Distill	Total	Fresh	Column Distill	Plant Distill	
13	Rosuvastatin Calcium	RVST1	360	285	48	72	14	4.0	0.83	3.3	Methanol (S-801)	1800	0	0	1800	100	0	0	
14											EA (S-811)	3385	5075	0	8460	40	60	0	
15											IPA (S-806)	136	0	0	136	100	0	0	
16	Atorvastatin Calcium	ATSC1	1000	1985	72	192	9.3	18.5	0.85	15.8	Cyclo Hexane (S-836)	2300	0	5370	7670	30	0	70	
17											IPA (S-806)	0	6600	0	6600	0	100	0	
18		ATSC2	560	490	24	48	28	13.7	0.97	13.4	Acetonitrile (S-810)	1120	1710	0	2830	40	60	0	
19											IPA (S-806)	143	0	0	143	100	0	0	
20		ATSC3	300	292	42	80	16	4.7	--	4.7	Methanol (S-801)	1360	0	0	1360	100	0	0	
21											Toluene (S-804)	0	0	3750	3750	0	0	100	

Solvent Input / Batch Details in Commercial Products @ LS-III

S. No	Product	Stage	B.Size (kg)	Output (kg)	BCF (Hrs)	Total Time Cycle (Hrs)	No. of batches /month	Stage Cap (TPM)	Yield Factor	API Eq. Cap (TPM)	Solvent	Quantity in (Lt / Batch)				Quantity in %			Remarks
												Fresh	Column Distill	Plant Distill	Total	Fresh	Column Distill	Plant Distill	
22	Pragabalin	AMHA1	862	1780	24	168	28	49.8	0.282672	14.1	Methanol (S-801)	1800	1500	0	3300	55	45	0	
23											Toluene (S-804)	400	0	4000	4400	9	0	91	
24		AMHA2	2000	1040	96	336	7	7.3	0.5436	4.0	Toluene (S-804)	0	0	7400	7400	0	0	100	
25											Ethyl Acetate (S-811)	0	0	1800	1800	0	0	100	
26		AMHA3 (Crude)	1600	1280	36	40	18.7	23.9	0.906	21.6	Toluene (S-804)	400	0	400	800	50	0	50	
27											Methanol (S-801)	800	0	0	800	100	0	0	
28		AMHA3 (Pure)		960	24	24	28.0	26.9			Methanol (S-801)	2200	0	5400	7600	29	0	71	
29		PGBN7	1000	480	72	168	9.3	4.5	0.906	4.1	Methanol (S-801)	1100	0	0	1100	100	0	0	
30											EA (S-811)	0	4000	0	4000	0	100	0	
31		PBLN4	500	453	24	42	28.0	12.7	--	12.7	IPA (S-806)	700	2000	0	2700	26	74	0	
32	Levetiracetam	LVTM2	600	585	60	144	11.2	6.6	--	6.6	MDC (S-807)	2500	5500	0	8000	31	69	0	
33											Acetone (S-805)	1500	0	0	1500	100	0	0	
												30524	**34635**	**43970**	**109129**	**28**	**32**	**40**	

Loss Quantity / Batch in Commercial Products @ LS-III

Loss Quantity / Batch in Commercial Products @ LS-III								
S.No	**Product**	**Stage**	**Solvent & S-Code**	**Input / Batch (Lts)**	**Spent Output (Lt / Batch)**	**Loss Qty / Batch**	**Loss % / Batch**	**Remarks**
1	Clopidogrel Bisulfate	CTPS1	Toluene (S-804)	1400	1200	200	14	
2			Cyclo Hexane (S-836)	2200	1550	650	30	
3		COPB1	Methanol (S-801)	2500	2000	500	20	
4			MDC (S-807)	2700	2080	620	23	
5			Methanol (S-801)	5000	4800	1584	32	
6			Acetone (S-805)	1080		576	53	
7		CGBH1	MDC (S-807)	1600	1010	590	37	
8			Toluene (S-804)	2000	1900	100	5	
9			IPA (S-806)	2850	2200	650	23	
10			EA (S-811)	3300	2200	1100	33	
11			Toluene (S-804)	2650	2100	550	21	
12		CGBH2	Methanol (S-801)	750	6000	750	100	
13			CH (S-836)	2000	1650	350	18	
14			Acetone (S-805)	2950	2200	750	25	
15	Rosuvastatin Calcium	RVST1	Methanol (S-801)	1800	1900	106	100	
16			EA (S-811) (Crude)	3060	2550	510	17	
17			IPA (S-806) (Pure-01)	136	0	136	100	
18			EA (S-811) (Pure-01)	5400	4450	950	18	

Loss Quantity / Batch in Commercial Products @ LS-III

S.No	Product	Stage	Solvent & S-Code	Input / Batch (Lts)	Spent Output (Lt / Batch)	Loss Qty / Batch	Loss % / Batch	Remarks
19	Atorvastatin Calcium	ATSC1	Cyclo Hexane (S-836)	4000	2700	1300	33	
20				1835	1480	355	19	
21				1835	1500	335	18	
22			IPA (S-806)	3300	2700	600	18	
23				3300	2750	550	17	
24		ATSC2	Acetonitrile (S-810)	2830	2700	130	5	
25			IPA (S-806)	143	0	143	100	
26		ATSC3	Methanol (S-801)	1360	3750	1360	100	
27			Toluene (S-804)	3750	3300	450	12	
28	Pragabalin	AMHA1	Methanol (S-801)	3300	2000	1300	39	
29			Toluene (S-804)	4400	4000	400	9	
30		AMHA2	Toluene (S-804)	7400	7000	400	5	
31			Ethyl Acetate (S-811)	1800	1350	450	25	
32		AMHA3 (Crude)	Toluene (S-804)	800	700	100	13	
33			Methanol (S-801)	800	680	120	15	
34		AMHA3 (Pure)	Methanol (S-801)	7600	5500	2100	28	
35		AMHA4	IPA (S-806)	2700	2050	650	24	
36		PGBN7	Methanol (S-801)	1100	580	520	47	
37			EA (S-811)	4000	3210	790	20	
38	Levetiracetam	LVTM2	MDC (S-807)	8000	6850	1150	14	
39			Acetone (S-805)	600	480	120	20	
40				900	705	195	22	
				109129	**95775**	**24190**	**22**	

Reuse Stages Solvent details

Reuse in Commercial Products @ LS-III								
S.No	**Product**	**Stage**	**Solvent & S-Code**	**Input / Batch (Lts)**	**Reuse (Lt / Batch)**	**Loss Qty / Batch**	**Further Treatment**	**Remarks**
1	Clopidogrel Bisulfate	CTPS1	Toluene (S-804)	1400	1200	200	Reuse	
2			Cyclo Hexane (S-836)	2200	1550	650	Reuse	
3		COPB1	MDC (S-807)	2700	2080	620	Reuse	
4		CGBH1	MDC (S-807)	1600	1010	590	Reuse	
5			Toluene (S-804)	2000	1900	100	Reuse	
6			EA (S-811)	3300	2200	1100	Reuse	
7			Toluene (S-804)	2650	2100	550	Reuse	
8		CGBH2	CH (S-836)	2000	1650	350	Reuse	
9	Atorvastatin Calcium	ATSC1	Cyclo Hexane (S-836)	4000	2700	1300	Reuse	
10				1835	1480	355	Reuse	
11				1835	1500	335	Reuse	
12		ATSC3	Toluene (S-804)	3750	3300	450	Reuse	
13	Pragabalin	AMHA1	Toluene (S-804)	4400	4000	400	Reuse	
14		AMHA2	Toluene (S-804)	7400	7000	400	Reuse	
15		AMHA3 (Crude)	Toluene (S-804)	800	700	100	Reuse	
16		AMHA3 (Pure)	Methanol (S-801)	7600	5500	2100	Reuse	
				49470	**39870**	**9600**		

SRS Treatment Stages Solvent details

To be Distilled in SRS Commercial Products @ LS-III										
S.No	**Product**	**Stage**	**Solvent & S-Code**	**Input / Batch (Lts)**	**Spent Output (Lt / Batch)**	**GC**	**MC**	**As such 100 %**	**Further Treatment**	**Remarks**
1	Clopidogrel Bisulfate	COPB1	MeOH (S-801)	2500	2000				To SRS	
2			MeOH (S-801)	5000	4800	S-801, 80%	20	2880	To SRS	
3			Acetone (S-805)	1080		S-805, 10%.		480		
4		CGBH1	IPA (S-806)	2850	2200	83	25	1276	To SRS	
5		CGBH2	Acetone (S-805)	2950	2200	97.4	3.5	2066	To SRS	
6	Rosuvastatin Calcium	RVST1	Methanol (S-801)	1800	1900	89.9	23	1271	To SRS	
7			EA (S-811) (Crude)	3060	2550	97.87	3	2419	To SRS	
8			EA (S-811) (Pure-01)	5400	4450	97.87	3	4222	To SRS	
9	Atorvastatin Calcium	ATSC1	IPA (S-806)	3300	2700	97.08	16.7	2170	To SRS	
10				3300	2750	97.08	16.7	2210	To SRS	
11		ATSC2	Acetonitrile (S-810)	2830	2700	95.2	28	1814	To SRS	
12	Pragabalin	AMHA1	Methanol (S-801)	3300	2000	91.51	8.12	1668	To SRS	
13		AMHA2	Ethyl Acetate (S-811)	1800	1350				To SRS	
14		AMHA3 (Crude)	Methanol (S-801)	800	680				To SRS	
15		AMHA4	IPA (S-806)	2700	2050	98	40	1189	To SRS	
16		PGBN7	Methanol (S-801)	1100	580				To SRS	
17			EA (S-811)	4000	3210				To SRS	
18	Levetiracetam	LVTM2	MDC (S-807)	8000	6850				To SRS	
19			Acetone (S-805)	600	480				To SRS	
20				900	705				To SRS	
				57270	**46155**					

Mixed Spent Solvent details

Mixed Spent 100% Loss in Commercial Products @ LS-III										
S.No	**Product**	**Stage**	**Solvent & S-Code**	**Input / Batch (Lts)**	**Process Output (Lts)**		**Recovery %**	**Loss %**	**Further Usage**	**Remarks**
					MLs	**Aqueous Layer**				
1	Clopidogrel Bisulfate	CGBH2	Methanol (S-801)	750	0	6000	0.0	100	ETP	
2	Atorvastatin Calcium	ATSC3	Methanol (S-801)	1360	3750	0	0	100	ETP	
3		ATSC2	IPA (S-806)	143	1100	0	0	100	ETP	
4	Rosuvastatin Calcium	RVST1	IPA (S-806) (Pure-01)	136	4450	0	0	100	Mixed loss	

Action plans for solvent minimization

Product		**Clopidogrel Bisulfate**	**Output / Batch (Lts)**	**1200**
Stage		**CTPS1**	**Recovery %**	**86**
Solvent		**Toluene (S-804)**	**Loss Qty / Batch (Lts)**	**200**
Input / Batch (Lts)		**1400**	**Loss % / Batch**	**14**
Distillation Loss	**Qty / batch**	~80		
	Reason			
	Action Plan			
Transfer Loss (charging, work-up, pumping)	**~ Saving Qty / batch**	~100		
	Reason	1) As per Process 2 Toluene extractions and 3 Water washings to OL. 2) Transferring the mass from one reactor to another reactor through vacuum. 3) S-804 is charging through Vacuum.		
	Action Plan	1) Additional Centrifugal pump & dedicated line is required to transfer the reaction mass, from one reactor to another reactor transferring the mass and to avoid losses in Vacuum. 2) Dedicated line required for S-804 Charging.		

Product		**Clopidogrel Bisulfate**	**Output / Batch (Lts)**	**1550**
Stage		**CTPS1**	**Recovery %**	**70**
Solvent		**Cyclo Hexane (S-836)**	**Loss Qty / Batch (Lts)**	**650**
Input / Batch (Lts)		**2200**	**Loss % / Batch**	**30**
Distillation Loss	**~ Saving Qty / batch**	~200		
	Reason	MLs Distillation in reactor with out chilled connection to Primary condenser.		
	Action Plan	Chilled Utility connection is required to Primary condenser.		
Transfer Loss (charging, work-up, pumping)	**Qty / batch**			
	Reason			
	Action Plan			
Filtration	**~ Saving Qty / batch**	~200		
	Reason	As per process after Isolation, product filtration through ANFD MLs receiver vacuum sucking and unloading in syntex and again transferring to reactor.		
	Action Plan	Direct 2" SS304 line to be arranged from ANFD to MLs Distillation Reactor with out MLs receiver, to avoid multiple transfers.		

Product		**Clopidogrel Bisulfate**	**Output / Batch (Lts)**	**2080**
Stage		**COPB1**	**Recovery %**	**77**
Solvent		**MDC (S-807)**	**Loss Qty / Batch (Lts)**	**620**
Input / Batch (Lts)		**2700**	**Loss % / Batch**	**23**
Distillation Loss	**~ Saving Qty / batch**	~300		
	Reason	Cooling loss is observed.		
	Action Plan	1) Required Jacketed Receiver with cooling facility to avoid Distillation loss. 2) Tertiary condenser with Brine circulation.		
Transfer Loss (charging, work-up, pumping)	**~ Saving Qty / batch**	~200		
	Reason	1) As per Process product is extracted in MDC. 2 times MDC extraction and 1 time Water washings to OL. 2) In extractions & Water washing to Reaction mass operation is transferring from one reactor to another reactor through vacuum.		
	Action Plan	1) Centrifugal pump & dedicated line is required to transfer the reaction mass, from one reactor to another reactor for transferring the mass and to avoid losses in Vacuum. 2) Dedicated line required for S-807 Charging.		

Product		**Clopidogrel Bisulfate**	**Output / Batch (Lts)**	**1010**
Stage		**CGBH1**	**Recovery %**	**63**
Solvent		**MDC (S-807)**	**Loss Qty / Batch (Lts)**	**590**
Input / Batch (Lts)		**1600**	**Loss % / Batch**	**37**
Distillation Loss	**~ Saving Qty / batch**	~300		
	Reason	Distillation under vacuum at below 35°C.		
	Action Plan	1) Avoid vacuum Distillation, if vacuum distillation means dedicated vacuum dry pump to be arranged. 2) Required Jacketed Receiver with cooling facility to avoid Distillation loss. 3) Tertiary condenser with Brine circulation.		
Transfer Loss (charging, work-up, pumping)	**~ Saving Qty / batch**	~200		
	Reason	1) As per Process product is extracted in MDC. 2 times MDC extraction and 1 time M-142 Water washings to OL. 2) In extractions & Water washing to Reaction mass operation is transferring from one reactor to another reactor through vacuum.		
	Action Plan	1) Additional Centrifugal pump is required for transferring the reaction mass through dedicated lines, from one reactor to another reactor to avoid losses in Vacuum. 2) Dedicated line required for S-807 Charging.		

Product		**Clopidogrel Bisulfate**	**Output / Batch (Lts)**	**1650**
Stage		**CGBH2**	**Recovery %**	**83**
Solvent		**Cyclo Hexane (S-836)**	**Loss Qty / Batch (Lts)**	**350**
Input / Batch (Lts)		**2000**	**Loss % / Batch**	**18**
Distillation Loss	**~ Saving Qty / batch**	~150		
	Reason	Distillation under vacuum at below 35°C.		
	Action Plan	1) Avoid vacuum Distillation, if vacuum distillation means dedicated vacuum dry pump to be arranged. 2) Chilled Utility connection is required to Primary condenser.		

Product		**Clopidogrel Bisulfate**	**Output / Batch (Lts)**	**2200**
Stage		**CGBH1**	**Recovery %**	**67**
Solvent		**EA (S-811)**	**Loss Qty / Batch (Lts)**	**1100**
Input / Batch (Lts)		**3300**	**Loss % / Batch**	**33**
Distillation Loss	**Qty / batch**	~270		
	Reason			
	Action Plan			
Transfer Loss (charging, work-up, pumping)	**~ Saving Qty / batch**	~630		
	Reason	1) As Per Process 5 vol (4000 Lts) of water is using for Dissolution and 1(800 Lts) Vol for pH adjustment after pH layer sepration. 2) 1 Vol (800 Lts) EA Extraction for Aq. Layer. 3) In CF MLs pH adjustment, layer seperation and 1 water washing.		
	Action Plan	1)As EA is soluble in water 8.3g/100ml (92 Lts EA soluble in 1000 Lts Water). Solubility Loss.		
Filtration	**~ Saving Qty / batch**	~200		
	Reason	Filteration loss is observed, filtration done in 4 lots.		
	Action Plan	Condenser with Utility connection is required.		

Product			**Output / Batch (Lts)**	**1650**
Stage		**CGBH1**	**Recovery %**	**64**
Solvent		**IPA (S-806)**	**Loss Qty / Batch (Lts)**	**915**
Input / Batch (Lts) As on 100%		**2565**	**Loss % / Batch**	**36**
Distillation Loss	**~ Saving Qty / batch**	~ 200 Lt		
	Reason	toluene + IPA mixture obtained from CF MLs, followed by Flash Distillation.		
	Action Plan	1) Chilled Brine Utility connection is required to secondary condenser. 2) During the flash distillation RM Temp. to be increased upto 95°C instead of 87°C, to minimize the residue quantity.		